REMARKS

In response to the Office Action of June 3, 2003, Applicants have amended the claims, which when considered with the following remarks, is deemed to place the present application in condition for allowance. Applicants have also added new claims 40-48 in order to further define the present invention. Favorable consideration of all pending claims is respectfully requested.

In the first instance, Applicants through the undersigned, thank Examiners Collins and Nelson for their time and consideration in granting a personal interview with the undersigned and representatives from CropDesign, NV, on October 14, 2003. Applicants additionally thank Examiner Collins for the helpful suggestions and guidance provided during the course of the interview where the Examiner indicated that the presently amended claims would be favorably considered.

Applicants acknowledge the withdrawal of the previously issued restriction requirement.

The Examiner has requested a newly executed oath because the previously-filed oath, although listing the relevant priority applications, did not contain a check mark in the box next to the statement that priority under 35 U.S.C.§ 119 was claimed. Submitted herewith is a newly executed oath that in addition to listing the relevant priority applications, also indicates by a check mark in the appropriate box, Applicants' claim for priority under 35 U.S.C. § 119.

The abstract has been objected to because it is not a single paragraph. In addition, the Examiner has objected to the abstract referring to an embodiment of the invention not claimed in this application. Submitted herewith on a separate sheet is a new abstract in a

single paragraph. Withdrawal of the objection to the specification is therefore respectfully requested.

Claims 23-39 have been rejected under 35 U.S.C.§ 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner's position is that the specification does not provide written support for plant cells and plants overexpressing the products of *any E2Fa* and *DPa* genes. Further, the Examiner believes that the specification lacks written support for the use of a multitude of non-exemplified regulatory genes or other non-*E2Fa* or non-*DPa* genes. In response to the rejection, and in order to advance prosecution of this application, claim 23 has been amended to recite: "[a] method for modulating endoreduplication in a plant or part thereof, which comprises transforming a plant cell with a native or heterologous coding sequence for a plant E2F protein operably linked to a promoter which functions in a plant cell, and regenerating a plant therefrom, wherein the plant E2F protein forms part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition of the cell cycle and wherein the transformed, regenerated plant exhibits an increase in endoreduplication compared to a corresponding wild type plant."

Claim 24 has been amended to recite: "[t]he method of claim 23 comprising further transforming the plant cell with a native or heterologous coding sequence for a plant Dp protein, operably linked to a promoter which functions in a plant cell and regenerating a plant therefrom, wherein the plant DP protein forms part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition of the cell cycle. Claim 27 has been amended to recite: "a plant having a plant cell which stably expresses the product of a plant *E2F* transgene wherein the expressed E2F protein

product forms part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition of the cell cycle." Claim 28 has been amended to recite: "[t]he plant of claim 27 having a cell which further expresses a product of a plant *DP* transgene wherein the expressed DP protein forms part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition of the cell cycle."

Claims 23-29 have also been rejected under 35 U.S.C. §112, first paragraph, as allegedly non-enabling. According to the Examiner, known *E2F* and *DP* sequences encode proteins having structural differences as well as similarities. For example, on page 7 of the Office Action, the Examiner sets forth differences among known plant and animal *E2F* and *DP* sequences. In response to the rejection and for purposes of advancing prosecution of this application, claims 23-29 presently recite "a plant E2F protein" or a "plant DP protein." Applicants respectfully submit that genes for other plant E2F and DP proteins were available as of the effective filing date of the present application and that one skilled in the art would reasonably believe the teaching of the present application, that the corresponding genes in other plant species would function similarly to Applicant's exemplified *Arabidopsis E2Fa* and *DPa* genes and transgenic *Arabidopsis* plants comprising such genes. For example, page 11 of the specification lists *E2F* coding sequences from various plants available at the time the application was filed, *to wit*, tobacco, wheat, carrot, and *Arabidopsis*. Page 11 of the specification also discloses two *Arabidopsis DPa* genes identified and characterized by Magyar et al. (2000) *FEBS Letts. 486*:79-87, one of which genes was employed in Example 16 of the present application. Further, page 11 of the specification discloses partial sequences from other plant *Dp* genes have been deposited in the genetic database, e.g., soybean *Dp*,

(Accession No. A1939068), tomato *DP* (Accession Number AW217514), and cotton *Dp* (Accession No. A1731675). Indeed, Magyar et al. in isolating *Arabidopsis* Dp genes, employed all three of the Dp partial sequences described above and referenced on page 11 of the specification.

Thus, as of the effective filing date of this CIP application, both E2F and DP plant nucleotide sequences were available for one skilled in the art to use in the methods and compositions of the present invention. Applicants also direct the Examiner to Albani et al. (2000), cited by the Examiner in the June 3, 2003 office action, and specifically cited in the specification of the present application, which reference provides information on a carrot E2F protein having extensive homology to that of wheat and tobacco E2F proteins, 50% and 54% homology, respectively. When the DNA-binding domains are examined among tobacco, wheat and human E2F proteins, a remarkable conservation of 75% amino acid identity is observed. *See* Figure 3 and page 19261 column 1, final paragraph of Albani et al. (2000). Albani et al. also disclose that the DP dimerization domain and the marked box domain are also well conserved in plant E2Fs Further, Albani et al. demonstrate that a carrot E2F is a functional transcription factor that can transactivate, together with a DP partner, an E2F-reporter gene in both plant and mammalian cells.

Moreover, Albani et al. demonstrate that a carrot E2F is capable of binding a human DP protein *in vivo*. Thus, not only has it been demonstrated that carrot E2F is a functional transcription factor that binds carrot DP, carrot E2F is also capable of binding a human DP *in vivo*. Applicants respectfully submit therefore, that one skilled in the art, having the present application and the relevant art in hand as of the effective filing date of the present application, would reasonably believe that various combinations of plant E2F

genes and DP genes could be used in different plants in order to practice the presently claimed invention. In addition, Applicants respectfully submit that a plant genome does not comprise a multitude of *E2F* or *DP* genes. Rather, out of the 30,000 or so genes in the Arabidopsis genome, there exist only 3 *E2F* genes and only 2 *DP* genes.

Based on the foregoing remarks, Applicants further submit that one skilled in the art would also reasonably believe that Applicants were in possession of the claimed invention as of the effective filing date of the present application. Withdrawal of the rejection of claims 23-29 under both the written description and enablement provisions of 35 U.S.C.§ 112, first paragraph, is therefore respectfully requested.

Claims 23-31 and 33 have been rejected under 35 U.S.C.§ 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, in claims 23 and 33, the Examiner finds recitation of "modulating" and "modulated" indefinite. The Examiner then gives a definition of the two terms with no indication from where the definition came. Applicants direct the Examiner to page 21, lines 1-3 of the specification, where it states that ""[m]odulation of expression or activity" means control or regulation, positively or negatively, of the expression or activity of a particular protein or nucleotide sequence by methods known to a skilled person." In order to advance prosecution of this application however, claim 23 has been amended to recite "increase in endoreduplication" rather than "modulated endoreduplication." Claim 33 retains the recitation of "modulated endoreduplication." Support for a subject plant having "modulated endoreduplication" may be found throughout the specification, e.g., as described above, i.e., on page 21 of the specification and also on page 40, where E2F/DP

transgenic plants are described as having *decreased* endoreduplication in cotyledon pavement cells and *increased* endoreduplication in cortical and palisade cells of the hypocotyls and cotyledon, respectively, and in mature trichome cells.

Claim 24 is allegedly indefinite for its recitation of "modifying the expression or activity of *E2Fa*." As presently amended claim 24 no loner recites this phrase.

Claims 23, 25, 26, 27, 29, 30, and 31 are also allegedly indefinite in reciting "*E2Fa*." Claims 23, 25, 26, and 27 as presently amended recite in relevant part: "wherein the plant E2F protein forms part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition of the cell cycle". Claims 29, 30 and 31 also recite the same since such claims depend from claims 23, 25, 26 and 27.

Claim 24 is allegedly indefinite in reciting "modifying the expression or activity of *DPa*." Claim 24 as presently amended, no longer recites this phrase.

Claims 24, 26, 28, and 31 are allegedly indefinite in reciting "DPa". In response to the rejection, claim 24 (and claims 26, 28, and 31 dependent thereon), presently recites in relevant part "wherein the plant DP protein forms part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition of the cell cycle."

Claims 25-28 and 31 have been found allegedly indefinite due to the recitation of "overexpressed" and "overexpressing." Applicants direct the Examiner to page 20, penultimate paragraph, where a definition of "expression" versus "overexpression" is provided. Specifically, this section of the specification discloses:

> "Expression" means the production of a protein or nucleotide sequence in the cell itself or in a cell-free system. It includes transcription into an RNA product, post-transcriptional modification and/or translation to a protein product or

> polypeptide from a DNA encoding the product, as well as possible post-translational modifications. In terms of increasing expression of a protein already made by a cell or cell-free system (i.e., a native protein), such expression may be also referred to as "overexpression" on account that the amount of gene product is due to transcription and translation of both the native and introduced coding sequence.

Claim 23 is presently amended to recite expression of a *E2Fa* transgene. Claims 25 and 26 retain the recitation of "overexpression." Claim 27 has been amended to recite "which stably expresses." Claim 28 has been amended to recite "which further stably expresses." In view of the amendments to claims 23-31 and 33 and the remarks hereinabove, withdrawal of the rejection of claims 23-31 and 33 under 35 U.S.C.§ 112, second paragraph, is warranted.

Claims 23-26 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite in being incomplete for omitting essential steps which amounts to a gap between the steps. In response to the rejection, claim 23 has been amended to recite in relevant part: "transforming a plant cell with a native or heterologous coding sequence for a plant E2F protein operably linked to a promoter which functions in a plant cell and regenerating a plant therefrom, wherein the plant E2F protein forms part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition of the cell cycle and wherein the transformed, regenerated plant exhibits an increase in endoreduplication compared to a corresponding wild type plant." Claim 24 has been amended to recite in relevant part: "further transforming the plant cell with a native or heterologous coding sequence for a plant DP protein operably linked to a promoter which functions in a plant cell, wherein the plant DP protein forms part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition in the cell

cycle and wherein the transformed, regenerated plant exhibits an increase in endoreduplication compared to a corresponding wild type plant." In view of the amendments to claims 23 and 24, withdrawal of the rejection of claims 23, 24 and claims 25 and 26, dependent thereon, under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claims 27-39 have been rejected under 35 U.S.C. §101 as allegedly directed to non-statutory matter. According to the Examiner, the rejected claims do not distinguish over naturally occurring plant cells and plants. Applicants respectfully direct the Examiner to page 20, last paragraph, of the present application, where a definition of "transgene" is provided. Further, in order to advance prosecution of this case, claim 27 has been amended to recite in relevant part: "[a] plant having a plant cell which stably expresses the product of a plant *E2F* transgene." Claim 28 has been amended to recite: "[t]he plant of claim 27 having a cell which further expresses a product of a plant *DP* transgene." Claim 29 has been amended to recite: "[t]he plant of claim 27 wherein the plant *E2F* transgene is heterologous to the plant." Claim 30 has been amended to recite: [t]he plant cell of claim 27 wherein the plant *EF2* transgene is native to the plant" Claims 31-33 depend from claims 27-30, which have been amended as described above. As suggested by the Examiner, claims 34 and 35 have been amended to recite that the transgenic progeny retain the transgene recited in the claims from which claims 34 and 35 depend. In view of the amendments to the claims and the remarks hereinabove, withdrawal of the rejection of claims 27-39 under 35 U.S.C. §101 is respectfully requested.

Claims 23-28 and 30-39 have been rejected under 35 U.S.C. §102(a) as allegedly anticipated by Magyar et al. (Nov. 16, 2000) *FEBS Letters 486*:79-87. Magyar et al. has been cited for its alleged teaching of a method of temporally modifying the expression or activity of *Arabidopsis E2Fa* and *Dpa*. The Examiner is apparently referring to the cell cycle phase-dependent gene transcription studies described on page 85 and Figure 4. Amended claims 23-28 and 30-39 require plant cell transformation with an *E2F* transgene or an *E2F/Dp* transgene combination, neither of which is disclosed in Magyar et al. Withdrawal of the rejection of claims 23-28 and 30-39 under 35 U.S.C.§ 102(a) is therefore warranted.

Claims 23, 25, 27, 30, and 32-39 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Albani et al. (June 2000) *Journal of Biological Chemistry, 275*(25):19258-19267. Albani et al. has been cited for its alleged teaching of a method of temporally modifying the expression or activity of a carrot *E2F*, including methods in which carrot *E2F* is overexpressed in a plant or plant part in comparison with its expression in other plant parts or at other times. Amended claims 23 and 25 require plant cell transformation with an *E2F* transgene or an *E2F/Dp* transgene combination, followed by regeneration of plants from the transformed cells. Although in performing transactivation studies, Albani et al. transformed carrot cells with a carrot E2F expression construct (p35S-DcE2F), no plants were regenerated from the transformed carrot cells. Thus, claims 23 and 25 as presently amended are distinguished from the teaching of Albani et al. Further, the carrot cells of Albani et al. transformed with p35S-DcE2F, *transiently* express a carrot E2F protein. *See* page 19260, column 1, where carrot cells are electroporated and page 19264, column 1, "[f]urthermore, transient expression of

either effector alone with pBI221-E2F did not increase the GUS activity considerably, but as shown in Figure 7B, co-expression of both DcE2F and DP1 effectors was able to transactivate efficiently pBI221-E2F via the six E2F binding sites, giving an increase in GUS expression of over 15-fold." In contrast, presently amended claims 27 and 30 recite a plant having a plant cell which *stably* express the product of a plant E2F transgene. Claims 27 and 30 as presently amended are therefore distinguished from the teaching of Albani et al. Support for stable transformation may be found throughout the specification, e.g., page 18, lines 21-31 and Example 16.

It is axiomatic that anticipation under section 102 requires that the prior art reference disclose *every element* of the claims. *In re King*, 801 F.2d, 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). Thus, there must be no difference between the subject matter of the claim and the disclosure of the prior art reference. Applicants respectfully submit that Applicants' plant having a cell which *stably* expresses a plant E2F is not the same as a transgenic plant cell which *transiently* expresses a plant E2F. Withdrawal of the rejection of claims 23, 25, 27, 30, and claims 32-39, dependent thereon, under 35 U.S.C.§ 102(a) is therefore warranted.

Claim 29 has been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Albani et al., in view of Ramirez-Parra et al. (1999) *Nucleic Acids Research 27*(17):3527-3533. In addition to the teaching provided Albani et al. as described above, Albani et al. is also cited for teaching that heterologous *E2F* genes from wheat and tobacco are known in the art and that the amino acid sequences of carrot, wheat, and tobacco are conserved in functionally significant regions such as the DNA binding domain and the *DP* dimerization domain. Ramirez-Parra has been cited for teaching the

deduced amino acid sequence of an *E2F* gene obtained from wheat that is heterologous to carrot cells taught by Albani et al.

According to the Examiner, Albani et al. also provide motivation for the transformation of plants to study the role of *E2Fa* in plants, as transformation studies conducted in animals indicate that at least one animal *E2F* is dispensable for cell proliferation" Office Action, page 14, first paragraph. Finally, the Examiner has stated in the last paragraph of the office action that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a plant cell that overexpresses the product of a heterologous *E2F* gene such as the wheat gene taught by Ramirez-Parra et al. or the tobacco *E2F* gene, without any surprising or unexpected results, as both DNA sequences encode antibodies" (*sic*, E2F proteins).

Applicants traverse the rejection of claim 29 under 35 U.S.C.§ 103(a) and respectfully submit the following. As presently amended, claim 29 recites: "[t]he plant of claim 27 wherein the plant *EF2* transgene is heterologous to the plant." As presently amended, claim 27 recites: "[a] plant having a plant cell which stably expresses the product of a plant *E2F* transgene wherein the expressed protein product forms part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition of the cell cycle."

It is respectfully submitted that there is no suggestion or motivation in Albani et al. or Ramirez-Parra et al. to produce a plant comprising a plant cell which stably expresses an *E2F* transgene. Albani et al. describe their contribution to the art on page 19259 as "taken together with these results" (i.e., the isolation of wheat and tobacco *E2F* homologs by Ramirez-Parra, 1999, the other reference upon which the rejection of claim

29 is based), "our data demonstrate that the *pRB/E2F* pathway is conserved in plants, and the isolation of plant *E2F* provides a new tool to understand how plant growth and development is controlled." There is no teaching or suggestion in Albani et al. for stable transformation of a plant cell with a heterologous *E2F* transgene since the transactivation experiments were carried out in carrot cells transformed with a carrot *E2F* transgene for transient expression in order to determine whether carrot E2F can function as a transcriptional activator. Nor is there any teaching or suggestion for regenerated plants from the transiently transformed carrot cells.

The deficiency of teaching provided in Albani et al. is not ameliorated by the disclosure of Ramirez-Para et al., who characterize their teaching as "the isolation, cloning and characterization of a wheat cDNA encoding a protein which interacts with a plant RBR protein..." page 3527, column 2, last paragraph, and "our studies reinforce the idea that G_1/S regulators in plants are unrelated to those of yeast cells but similar to those of animal cells and provide new tools to analyse the links between cell cycle regulators, plant growth and developmental signals." Ramirez-Para et al. do not suggest stable transformation of a plant cell with a heterologous *EF2* transgene. There is no suggestion in either reference, taken alone or in combination for a plant having a plant cell which stably expresses a heterologous E2F. There is certainly no motivation to express a heterologous *E2F* transgene in a plant cell since neither reference taken alone or in combination suggests what effects such expression might have on a plant cell.

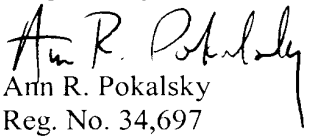
At most, the combination of teachings provided by Albani et al. and Ramirez-Para et al., might provide an invitation to experiment, i.e., might render the subject matter of claim 29 as obvious to try. "Obvious to try", however, is not the proper standard under

35 U.S.C.§ 103(a). *In re Fine*, 837 F.2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988). Withdrawal of the rejection of claim 29 under 35 U.S.C. § 103(a) is therefore respectfully requested.

As indicated in the first paragraph under the "Remarks" section, claims 40-46 have been newly added. Support for newly added claim 40 may be found throughout the specification, e.g., page 41 and Table 2. Support for newly added claims 41, 42, 43, 44 may be found throughout the specification, e.g., page 41, and Table 2. Support for newly added claim 45 may be found throughout the specification, e.g., page 40. Support for newly added claim 46 may be found throughout the specification, e.g., page 11.

Accordingly, in view of the amendments to the claims and the foregoing remarks, the present application is believed to be in condition for allowance, which action is earnestly solicited. The Examiner is invited to telephone the undersigned to resolve any remaining issues in this application as expeditiously as possible, e.g. by Examiner's amendment.

Respectfully submitted,



Ann R. Pokalsky
Reg. No. 34,697
Attorney for Applicants

DILWORTH & BARRESE
333 Earle Ovington Blvd.
Uniondale, NY 11553
(516) 228-8484
ARP:bg

Enclosure: Abstract of the Disclosure
Inventors' Declaration